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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,631	01/28/2004	Zhong Zhang	TPIP018X2	3752

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,631	ZHANG ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 10-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed November 8, 2005 presents remarks and arguments. Claims 1 and 10-74 are pending in the application. Applicant request for reconsideration of the rejection of claims in the last office action has been considered.

Status of claims

Claims 1, 10-74 is pending.

Claims 2-9 are cancelled.

Claims 1, 10-74 are rejected.

Response to Arguments

In response to the Office action dated November 8, 2005, Applicant has provided arguments for patentability of claims 1, 10-74 in the transmittal of a response to August 11, 2005 Office Action.

Objection to the specification

The objection to the specification has been withdrawn for the reasons in Applicants response on page 42.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejection under Claim Rejections - 35 USC § 102

Applicant's arguments, see page s 42-43, filed November 8, 2005, with respect to claims 1 and 2 have been fully considered and are persuasive. The rejection of claims 1and 2 has been withdrawn.

Rejection under Claim Rejections - 35 USC § 103

Applicant's arguments filed November 8, 2005 have been fully considered but they are not persuasive. As stated to page 45-

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *See* M.P.E.P. § 2143.

47 . A prima facia evidence was established by combining the references of the stated prior art. Even though Glen et al. did not explicitly teach the block copolymer to be 6-8 % as claimed by Applicant, it however teaches a range which overlaps the Applicants' claimed invention. The patent teaches (see col. 3 lines lines 27-28 a block copolymer from 5-20%. It is well within the level of one skilled in the art to be motivated to determine the optimum concentration/dosage to get the maximum effect. Hence the reference makes obvious the instant claim invention.

New Rejection under Claim Rejections - 35 USC § 102

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Glen et al., US 4,056,635.

Glen et al teach the instant claim 1 an aqueous formulation comprising:

a. block copolymer (see col.3 lines 26-27),

b. a polyethylene glycol (see col. 3 lines 29-30)

c. 2,6-diisopropylphenol (see col. lines 22-23)

d. propylene glycol (see col. 2 lines 29-35) In addition to the claim limitation a-c and e, Glen discloses a suitable additional solvent propylene.

e. water (see col. 3 lines 30).

New Rejection under Claim Rejections - 35 USC § 103

Claims 1, 10-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,056,635 in view of Meadow et al., WO 03/017977 A1.

Glen et al teach the instant claim 1 an aqueous formulation comprising:

a. block copolymer (see col.3 lines 26-27),

b. a polyethylene glycol (see col. 3 lines 29-30)

c. 2,6-diisopropylphenol (see col. lines 22-23)

d. propylene glycol (see col. 2 lines 29-35) (In addition to the claim limitation a-c and e, Glen discloses a suitable additional solvent propylene).

e. water (see col. 3 lines 30).

Claims 10 and 11, where the total amount of the block polymer is from 5-10% of said formulation (see col. 3 lines 27-28) an over lap of the range exist, therefore will be

obvious to one of ordinary skill to modify to achieve the instantly claimed invention. Claim 10 recites from less than 10% and claim 11 recites 5-10%.

Claims 13 where the block copolymer –is a poloxamer (pluronic 68 see col. 3 lines 27-28). Poloxamers are block copolymer therefore meets the limitation.

With regards to claim 16 and 20, Glen et al. also teaches the amount of 2,6-diisopropylphenol is 1% (see col. 3 line 65), in claim 18 the 2,6-diisopropylphenol is from 1-5% (see col. 3 line 62), and in claim 19, the 2,6-diisopropylphenol is 1-2 % is recited at (see col. 3 lines 62-66).

Claim 21 and 22, the PEG is 10 %(which is included in the range up to 15%), therefore the claim limitations of 21 and 22 are met (see col. 6 line 7-8). Also the Glen et al teach PEG-400 (see col. 2 lines 35-36) as in claims 27 and 28.

As to claims 23-26 and 29-31 the Glen reference teach the range of a non-ionic surfactant 2-30% overlaps the claim limitations in claims 29-31.

Meadow et al. teaches claims 14 and 15 the poloxamer188 (see page 2 third paragraph).

The instant invention differs from that disclosed in the reference in the particular poloxamer used. One skilled in the art would be motivated to employ the poloxamer 188 of the meadow et al. and expect the same result because block copolymers are used in the pharmaceutical industry as micelles of drug carriers, therefore switching, the block polymer would not have affected the claimed subject matter.

With regards to the specific amount limitations in claims 23-26 and 29-31, the determination of the optimum range is well within the level of one having ordinary skill in

the art and the skilled artisan would be motivated to determine optimum amounts to get the maximum effect of the drug. Hence the reference makes obvious the instant claim invention.

Claims 32-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,056,635 in view of Meadow et al., WO 03/017977 A1 as applied to claims 1-10-31 above, and further in view of May et al., US 6,140,374 and Lee et al., US 6,743,436 B1.

Glen et al., and Meadow et al., are applied here as stated in the above rejection. In addition Glen teaches current claim 32 contains citric acid in the composition (see col. 9 lines 12-14). Glen also teaches the formulation is administered to a mammal (see col.1 lines 5-7) to induce anesthesia recited in claim 73. Claim 74 is obvious, as the formulation will comprise a container.

May et al. teach current claims 35, 36, 60-61 pharmaceutical formulation containing an antimicrobial agent –benzyl alcohol (see abstract), in an amount 0.0175-0.9% (see col. 2 lines 28-45) as in claim 37. As to claim 39, 2,6-diisopropylphenol is recited as 1 and 2% w/v of said formulation (see col. 2 line 14) and 1% by w/v (see col. 2 line 16) as in claims 40-48, 51-55.

As to claim 49, 66 and 72, Lee teaches the block copolymer is less that 10 % (see cols. 7 and 8). Lee et al. also teach an aqueous solution containing a poloxamer 188 in an amount of 8% (see col. 7 line 32+) in claims 51and 52, and 7% as recited in claims (see 6 line 65+). Also the reference teaches the range of PEG from 0.5-5% (see col.7 lines 16-65) as recited in claims 39-57.

The lee reference also teaches the formulation contains polysorbate (see col. 7 lines 47-50) recited in claim 62. The polyoxyethylene 20 sorbitan is present in 2% (see col. 7 lines 47-50) in claim 63.

Although Glen et al. did not state the concentration of the citric acid as disclosed in the instant application, the use of citric aid is to maintain the pH of the composition, therefore one of ordinary skill in the art will modify the concentration of the acid to achieve the desired pH level of the formulation.

Also the combine above reference teaches a wide concentration range for copolymers, PEG, citric acid. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a sterile composition ranges replace the concentration as disclosed in the 635 patent with that of the applicant as the formulation contains all the necessary components for anesthesia in a patient. Although, Glen did not per se teach of the exact concentration of the components, Lee, however provided motivation to optimize the ranges of surfactants used with the lipid, based upon the examples given (see col. 6), where 4 grams of the surfactant and 0.5 g of PEG versus, 8 grams surfactant and 5 grams PEG, indicating concentration ranges can be optimized, based, upon the lipid use as soluble lipid-soluble drugs are generally poorly soluble in water and possesses limitation as disclosed by Lee et al. (col. 1 line 64+). Lee further explained (see col. 5. line 4+), the effect of selecting a suitable surfactant to increase the surface tension. As to the poloxamer 237 in claim 65, one skilled in the art would have been motivated to employ the poloxamer, because the above cited

references teach a wide variety of poloxamers used in to achieve the instantly claimed subject matter.

One of ordinary skill in the ad would have been motivated to combine the teachings of Glen with that of Meadow et al. May et al. and Lee et al. which result in the concentrations as claimed and obtained successful results in administering the formulation as an anesthetic to patients. One of the ordinary skills in the art would have known administering anesthesia to patients would vary as to tolerance, and the condition of the patient in need. It would have been obvious to one of ordinary skill in the ad to add an antimicrobial to the solution to prevent microbial growth in compositions intended for human and/or veterinary use. Therefore the skilled artisan would have incorporated an anti bacterial agent to the formulation.
One of ordinary skill in the art would have expected successful results and would have been motivated combining the teachings of the above cited references as the art recognizes the claimed formulation (claim 1) for use as an anesthesia.

Lastly, it would have been obvious to one of ordinary skill in the art to use a purified poloxamer, since the formulation is intended for human.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
2/3/06

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